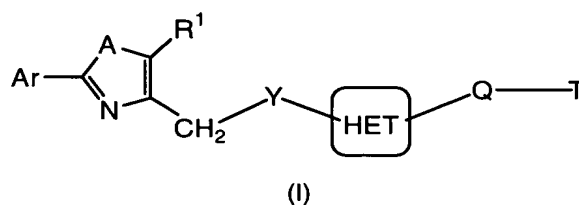


What is claimed:

1. A compound of formula (I):



wherein:

Ar is (C₃-C₁₀)cycloalkyl, (C₂-C₁₀)heterocyclyl, (C₆-C₁₀)aryl, or (C₁-C₁₀)heteroaryl, wherein each Ar is optionally substituted with one to four substituents selected from Z;

A is -CH₂-, -NH-, -O-, or -S-;

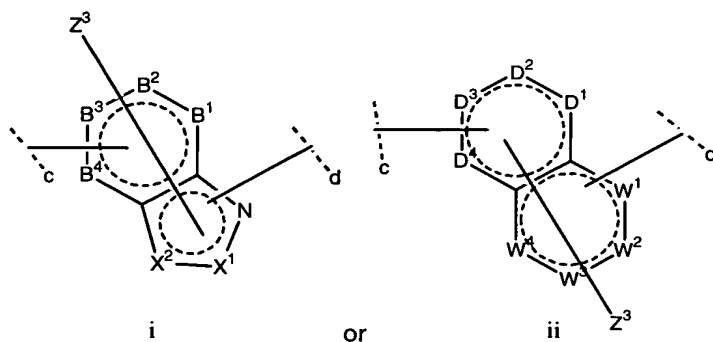
R¹ is (C₁-C₈)alkyl, (C₃-C₁₀)cycloalkyl, (C₂-C₁₀)heterocyclyl, (C₆-C₁₀)aryl, or (C₁-C₁₀)heteroaryl; wherein each R¹ is optionally substituted with one to four substituents selected from Z¹;

Y is selected from the group consisting of -(CH₂)_n-, -(CH₂)_n-NR¹⁵-, -(CH₂)_n-O-, and -(CH₂)_n-S-; wherein each n is independently 0, 1, 2, or 3;

and R¹⁵ is hydrogen, (C₁-C₈)alkyl, (C₃-C₁₀)cycloalkyl, (C₂-C₁₀)heterocyclyl, (C₆-C₁₀)aryl, or (C₁-C₁₀)heteroaryl; wherein each R¹⁵ is optionally substituted with one to four substituents selected from Z²;

Q is selected from the group consisting of -(CR²R³)_m-, -(CR²R³)_m-N¹⁵-, -N¹⁵-(CR²R³)_m-, (CR²R³)_m-O-, -O-(CR²R³)_m-, -S-(CR²R³)_m-, and -(CR²R³)_m-S-; wherein each m is independently 1, 2, 3, 4, 5, or 6;

HET is a fused (C₆-C₁₂)heteroaryl optionally substituted one to four substituents selected from Z³, wherein Z³ may be in any ring of the fused (C₆-C₁₂)heteroaryl, having the formula:



wherein the dotted lines are optional double bonds such that said fused

(C₆-C₁₂)heteroaryl is aromatic;

Each of X¹, X², W¹, W², W³, W⁴, B¹, B², B³, B⁴, D¹, D², D³ and D⁴ are independently =CH- or =N-;

5 At least one of X¹, X², B¹, B², B³, and B⁴ must be =N-;

At least one of W¹, W², W³, W⁴, D¹, D², D³ and D⁴ must be =N-;

Wherein each --c is a point of attachment to the group -Y- and each ---d is a point of attachment to the group -Q-;

Each of Z, Z¹, Z², and Z³ are selected from the group consisting of:

10 (c) H, F, Cl, Br, I, CF₃, or CN;

(d) (C₁-C₈)alkyl optionally substituted with one to four substituents independently selected from R⁷;

(c) -C(=O)-R⁴ {wherein R⁴ is selected from the group consisting of H, OH, CF₃, (C₁-C₈)alkyl, (C₁-C₈)alkyl-O-, (C₃-C₁₀)cycloalkyl, (C₃-C₁₀)cycloalkyl-O-, (C₂-C₁₀)heterocyclyl, (C₂-C₁₀)heterocyclyl-O-, (C₆-C₁₀)aryl, (C₆-C₁₀)aryl-O-, (C₁-C₁₀)heteroaryl, and (C₁-C₁₀)heteroaryl-O-};

15 (d) -C(=O)-NR⁵R⁶ {wherein R⁵ is H or (C₁-C₈)alkyl; and wherein R⁶ is selected from the group consisting of H, (C₁-C₈)alkyl, -CH₂-(C=O)-O-(C₁-C₈)alkyl, (C₃-C₁₀)cycloalkyl, (C₂-C₁₀)heterocyclyl, (C₆-C₁₀)aryl, and (C₁-C₁₀)heteroaryl};

20 (j) (C₃-C₁₀)cycloalkyl, (C₂-C₁₀)heterocyclyl, (C₆-C₁₀)aryl, or (C₁-C₁₀)heteroaryl;

(k) NR⁹R¹⁰ {wherein R⁹ is independently H or (C₁-C₈)alkyl; R¹⁰ is selected from the group consisting of -C(=O)-O-C(CH₃)₃, (C₁-C₈)alkyl, (C₃-C₁₀)cycloalkyl, (C₂-C₁₀)heterocyclyl, (C₆-C₁₀)aryl, and (C₁-C₁₀)heteroaryl; or R⁹ and R¹⁰ may optionally be taken together with the nitrogen to which they are attached to form a 5 to 8-membered heteroaryl or heterocyclyl ring};

25 (l) R¹¹-O- {wherein R¹¹ is selected from the group consisting of (C₁-C₈)alkyl, (C₃-C₁₀)cycloalkyl, (C₂-C₁₀)heterocyclyl, (C₆-C₁₀)aryl, and (C₁-C₁₀)heteroaryl};

(m) R¹²-SO_p- {wherein R¹² is selected from the group consisting of (C₁-C₈)alkyl, (C₃-C₁₀)cycloalkyl, (C₂-C₁₀)heterocyclyl, (C₆-C₁₀)aryl, and (C₁-C₁₀)heteroaryl; and wherein p is 0, 1, or 2}; and

30 (n) R¹³R¹⁴N-SO_q- {wherein R¹³ is H or (C₁-C₈)alkyl; R¹⁴ is (C₁-C₈)alkyl, (C₃-C₁₀)cycloalkyl, (C₂-C₁₀)heterocyclyl, (C₆-C₁₀)aryl, or (C₁-C₁₀)heteroaryl; or R¹³ and R¹⁴ may optionally be taken together with the nitrogen to which they are attached to form a 5 to 8-membered heteroaryl or heterocyclyl ring; and wherein q is 1 or 2};

35 Each of R² and R³ is independently (a) H; (b) (C₁-C₈)alkyl optionally substituted with one to four substituents independently selected from R⁷; (c) COOH; or (d) (C₆-C₁₀)aryl optionally substituted with one to four substituents independently selected from R⁸;

Wherein each of R⁷ and R⁸ are independently selected from the group consisting of:

(g) F, Cl, Br, I, CN, CF₃, or NO₂;

(h) -NR⁹R¹⁰ {wherein R⁹ is independently H or (C₁-C₈)alkyl; R¹⁰ is selected from the group consisting of -C(=O)-O-C(CH₃)₃, (C₁-C₈)alkyl, (C₃-C₁₀)cycloalkyl, (C₂-C₁₀)heterocyclyl, (C₆-C₁₀)aryl, and (C₁-C₁₀)heteroaryl; or R⁹ and R¹⁰ may optionally be taken together with the nitrogen to which they are attached to form a 5 to 8-membered heteroaryl or heterocyclyl ring};

(i) R¹¹-O- {wherein R¹¹ is selected from the group consisting of (C₁-C₈)alkyl, (C₃-C₁₀)cycloalkyl, (C₂-C₁₀)heterocyclyl, (C₆-C₁₀)aryl, and (C₁-C₁₀)heteroaryl};

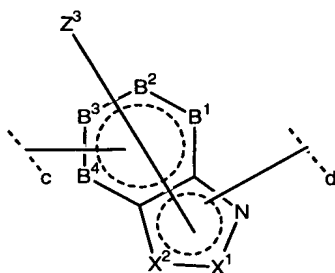
(j) R¹²-SO_p- {wherein R¹² is selected from the group consisting of (C₁-C₈)alkyl, (C₃-C₁₀)cycloalkyl, (C₂-C₁₀)heterocyclyl, (C₆-C₁₀)aryl, and (C₁-C₁₀)heteroaryl; and wherein p is 0, 1, or 2}; and

(k) R¹³R¹⁴N-SO_q- {wherein R¹³ is H or (C₁-C₈)alkyl; R¹⁴ is (C₁-C₈)alkyl, (C₃-C₁₀)cycloalkyl, (C₂-C₁₀)heterocyclyl, (C₆-C₁₀)aryl, or (C₁-C₁₀)heteroaryl; or R¹³ and R¹⁴ may optionally be taken together with the nitrogen to which they are attached to form a 5 to 8-membered heteroaryl or heterocyclyl ring; and wherein q is 1 or 2};

(l) T is selected from the group consisting of -(C=O)-OH, -(C=O)-OR¹⁵, -(C=O)-OM {wherein M is an alkali metal or alkaline earth metal}, tetrazolyl, thiazolidinyl, -SO₂-NH-R¹⁵, -NH-SO₂-R¹⁵, -(C=O)-NH-SO₂-R¹⁵, and other acid prodrug or isosteres thereof; or a pharmaceutically acceptable salt thereof.

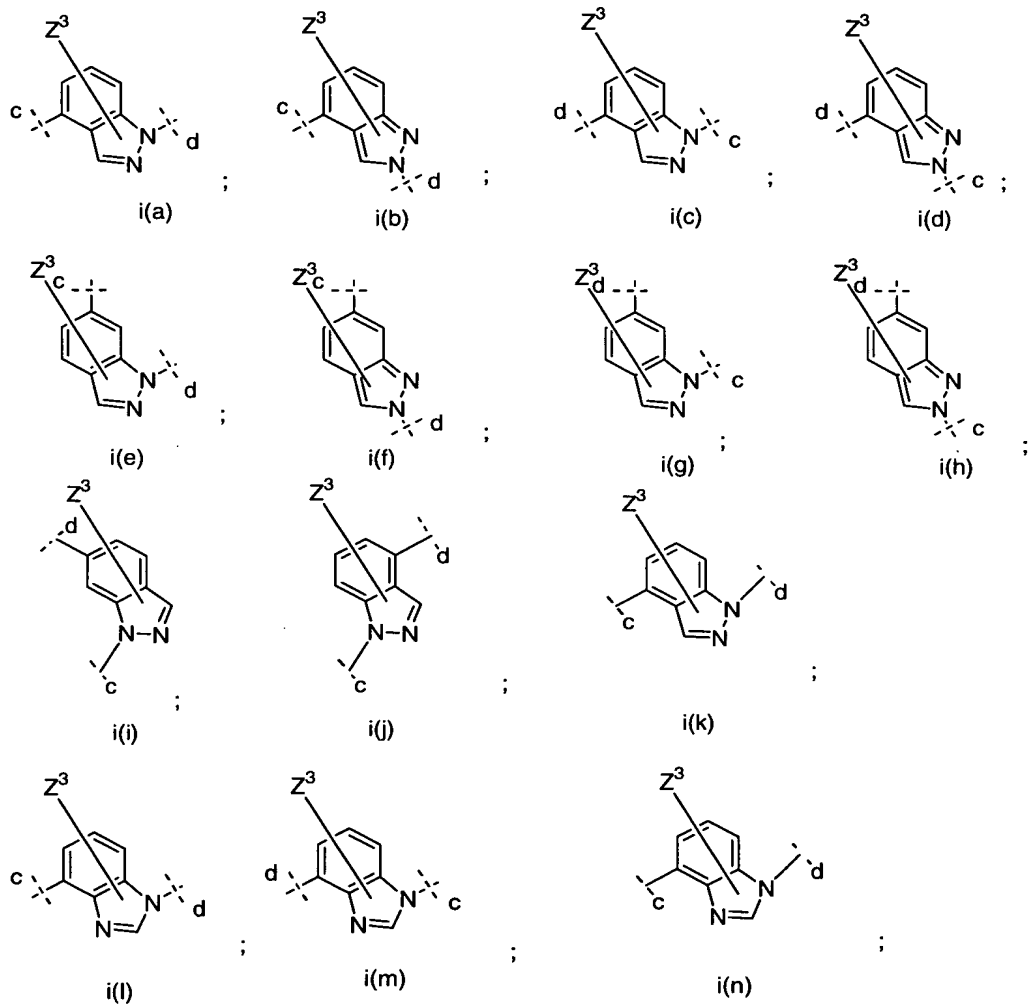
2. The compound according to claim 1 wherein

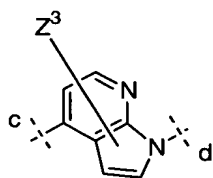
(HET) is a fused (C₆-C₁₂)heteroaryl optionally substituted one to four substituents selected from Z³, wherein Z³ may be in any ring of the fused (C₆-C₁₂)heteroaryl, having the formula:



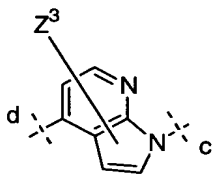
i

selected from the group consisting of:

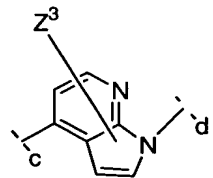




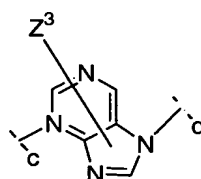
i(o)



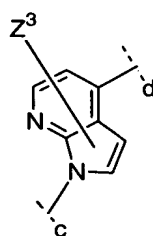
i(p)



i(q)



i(r)



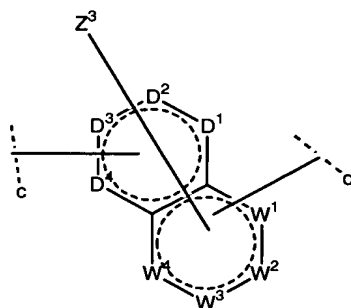
i(s)

3. The compound according to claim 1 wherein

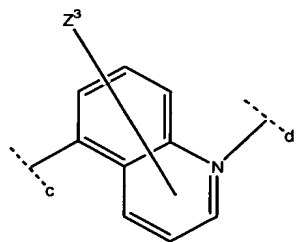
HET

is a fused (C₆-C₁₂)heteroaryl optionally substituted one to four substituents selected from Z³, wherein Z³ may be in any ring of the fused (C₆-C₁₂)heteroaryl, having the

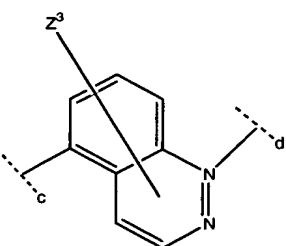
5 formula:



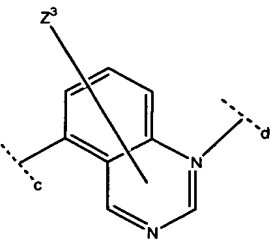
selected from the group consisting of:



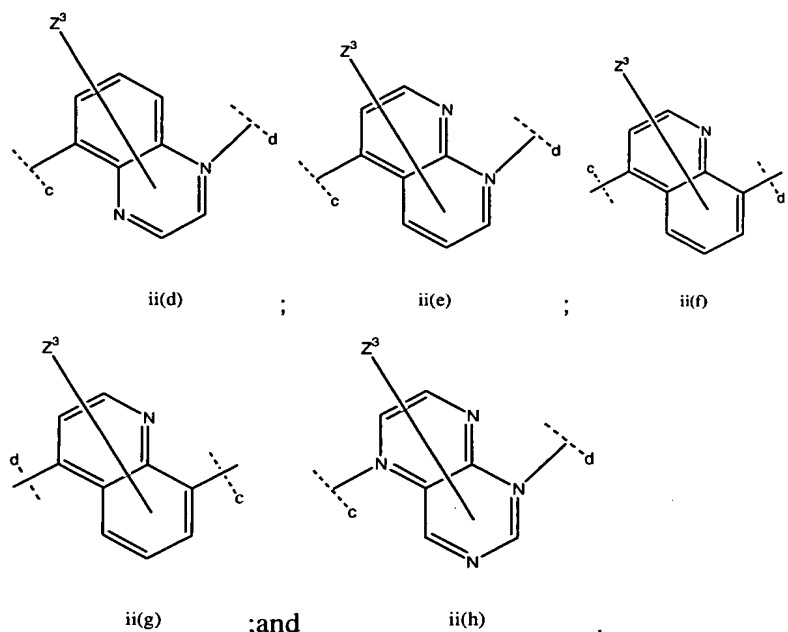
ii(a)



ii(b)

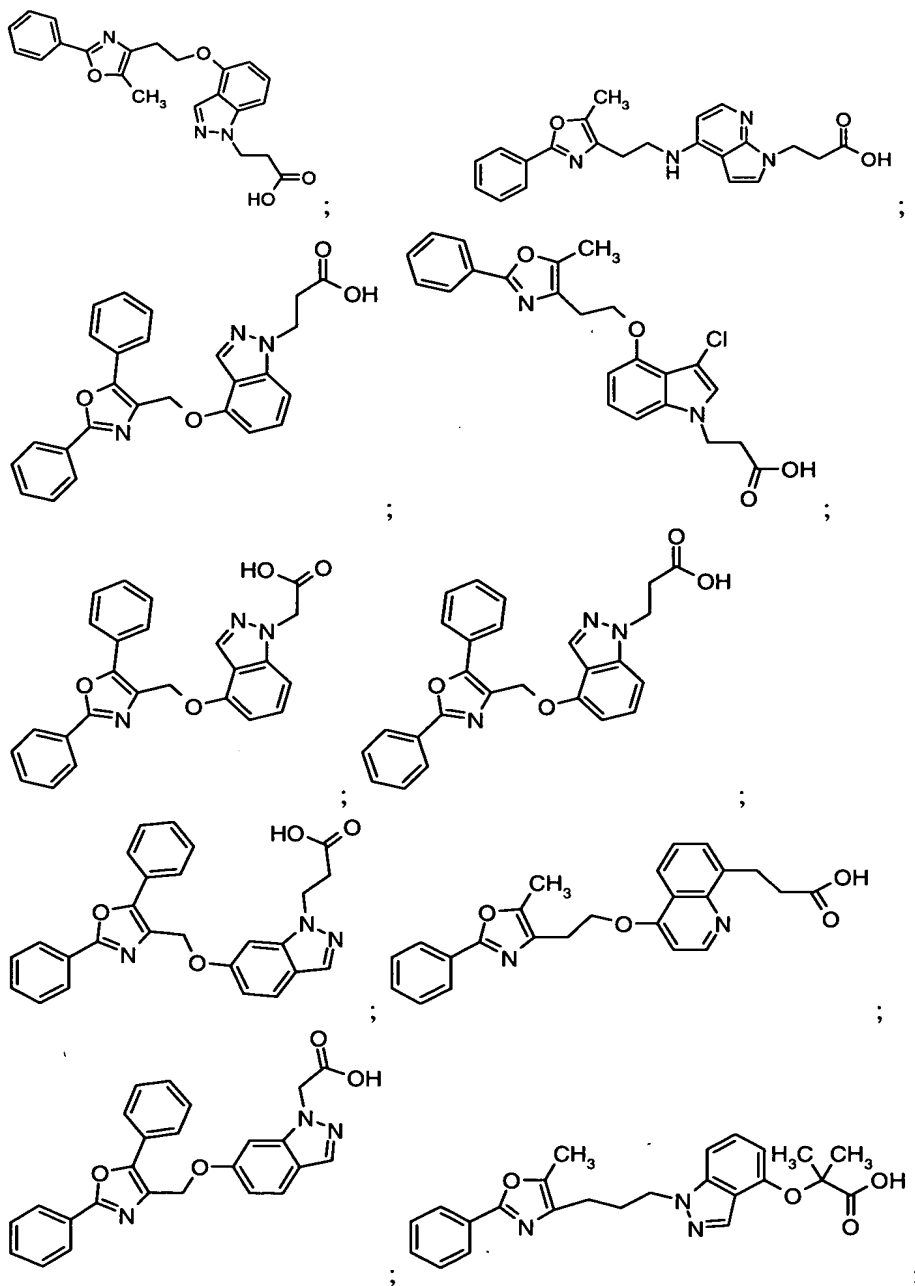


ii(c)



4. The compound according to claim 1 wherein said Ar is phenyl.
5. The compound according to claim 1 wherein said A is —O—.
- 5 6. The compound according to claim 1 wherein said R¹ is (C₁-C₈)alkyl.
7. The compound according to claim 1 wherein said R¹ is (C₆-C₁₀)aryl.
8. The compound according to claim 1 wherein said Q is —(CR²R³)_m—, m is 2 or 3, and each of R² and R³ is hydrogen or (C₁-C₈)alkyl.
9. The compound according to claim 1 wherein said Q is —(CR²R³)_m-NH—, m is 1 or 2, and each of R² and R³ is hydrogen or unsubstituted (C₁-C₈)alkyl.
- 10 10. The compound according to claim 1 wherein said Q is —(CR²R³)_m-O—, m is 1 or 2, and each of R² and R³ is hydrogen or unsubstituted (C₁-C₈)alkyl.
11. The compound according to claim 1 wherein said Q is —(CR²R³)_m-S—, m is 1 or 2, and each of R² and R³ is hydrogen or unsubstituted (C₁-C₈)alkyl.
- 15 12. The compound according to claim 1 wherein said T is —(C=O)-OH.
13. The compound according to claim 1 wherein said T is selected from the group consisting of tetrazolyl, thiazolidinyl, —SO₂-NH-R¹⁵, —NH-SO₂-R¹⁵, —(C=O)-NH-SO₂-R¹⁵, and other acid prodrug or isosteres thereof.
14. The compound according to claim 1 wherein said Z³ is selected from the group consisting of F, Cl, Br, or I.
- 20 15. The compound according to claim 1 wherein said Z³ is (C₁-C₈)alkyl.
16. The compound according to claim 1 wherein said Y is —(CH₂)_n-O— and n is 1, 2, or 3.

17. The compound according to claim 1 wherein said Y is $-(CH_2)_n-NR^{15}-$, wherein R^{15} is hydrogen, (C_1-C_8) alkyl or (C_3-C_{10}) cycloalkyl, and n is 1, 2, or 3.
18. The compound according to claim 1 wherein said Y is $-(CH_2)_n-$ and n is 1, 2, or 3.
19. The compound according to claim 1 wherein said Y is $-(CH_2)_n-S-$ and n is 1, 2, or 3.
- 5 20. The compound according to claim 1 selected from the group consisting of:



and the pharmaceutically acceptable salts thereof.

21. A method of treating non-insulin dependent diabetes mellitus in a mammal comprising administering to the mammal in need thereof a therapeutically effective amount of a fused heteroaryl compound according to claim 1.
- 5 22. The method of treating non-insulin dependent diabetes mellitus according to claim 21 wherein said mammal has an impaired glucose tolerance.
23. A method of treating polycystic ovarian syndrome in a mammal comprising administering to the mammal in need thereof a therapeutically effective amount of a fused heteroaryl compound according to claim 1.
- 10 24. A method of treating obesity in a mammal comprising administering to the mammal in need thereof a therapeutically effective amount of a fused heteroaryl compound according to claim 1.
25. A method of reducing body weight in an obese mammal comprising administering to the mammal in need thereof a therapeutically effective amount of a fused heteroaryl compound
- 15 according to claim 1.
26. A method of treating hyperglycemia in a mammal comprising administering to the mammal in need thereof a therapeutically effective amount of a fused heteroaryl compound according to claim 1.
27. A method of treating hyperlipidemia in a mammal comprising administering to the
- 20 mammal in need thereof a therapeutically effective amount of a fused heteroaryl compound according to claim 1.
28. A method of treating hypercholesteremia in a mammal comprising administering to the mammal in need thereof a therapeutically effective amount of a fused heteroaryl compound according to claim 1.
- 25 29. A method of treating atherosclerosis in a mammal comprising administering to the mammal in need thereof a therapeutically effective amount of a fused heteroaryl compound according to claim 1.
30. A method of treating hypertriglyceridemia in a mammal comprising administering to the mammal in need thereof a therapeutically effective amount of a fused heteroaryl compound
- 30 according to claim 1.
31. A method of treating hyperinsulinemia in a mammal comprising administering to the mammal in need thereof a therapeutically effective amount of a fused heteroaryl compound according to claim 1.
- 35 32. A method of treating a patient suffering from abnormal insulin and/or evidence of glucose disorders associated with circulating glucocorticoids, growth hormone, catecholamines, glucagon, or parathyroid hormone, comprising administering to said patient a therapeutically effective amount of a fused heteroaryl compound according to claim 1.

33. A method of treating insulin resistance syndrome in humans comprising administering to a patient in need of treatment a therapeutically effective amount of a fused heteroaryl compound according to claim 1.
- 5 34. A method of treating PPAR-related disorders in humans comprising administering to a patient in need of treatment a therapeutically effective amount of a fused heteroaryl compound according to claim 1.
35. A method of modulating PPAR activity in a mammal, comprising administering to a mammal a therapeutically effective amount of a fused heteroaryl compound according to claim 1.
- 10 36. A method of lowering blood glucose in a mammal, comprising administering to a mammal an amount of a fused heteroaryl compound according to claim 1 effective to lower blood glucose levels.
37. A method of modulating fat cell differentiation in a mammal, comprising administering to a mammal a therapeutically effective amount of a fused heteroaryl compound according to claim 1.
- 15 38. A method of modulating processes mediated by PPAR in a mammal, comprising administering to a mammal a therapeutically effective amount of a fused heteroaryl compound according to claim 1.
39. The method of modulating processes mediated by PPAR in a mammal according to claim 39, wherein said fused heteroaryl compound according to claim 1 is administered to said mammal in combination with at least one compound selected from the group consisting of α -glucosidase inhibitors, aldose reductase inhibitors, biguanide preparations, statin base compounds, squalene synthesis inhibitors, fibrate base compounds, LDL catabolism promoters and angiotensin-converting enzyme inhibitors.
- 20 40. A method of increasing insulin sensitivity in mammals, comprising administering to a mammal a therapeutically effective amount of a fused heteroaryl compound according to claim 1.
41. A composition comprising at least one modulator of PPAR according to claim 1 and a pharmaceutically acceptable carrier thereof.
- 30 42. A composition according to claim 40 further comprising at least one compound selected from the group consisting of α -glucosidase inhibitors, aldose reductase inhibitors, biguanide preparations, statin base compounds, squalene synthesis inhibitors, fibrate base compounds, LDL catabolism promoters and angiotensin-converting enzyme inhibitors.